FORM PTO-1390 (REV. 9-2001) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY 'S DOCKET NUMBER: PST6220P1US/2168

U.S APPLICATION NO. (If known, see 37 CFR 1.5): 10/030886

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP00/03513	17 April 2000	12 May 1999

TITLE OF INVENTION: **A COMPOSITION CONTAINING CARVACROL AND THYMOL FOR USE AS A BACTERICIDE**

APPLICANT(S) FOR DO/EO/US: Riccardo Losa

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [X] This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. [ ] The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [ ] is attached hereto (required only if not communicated by the International Bureau).
   b. [X] has been communicated by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [X] An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. [ ] is attached hereto.
   b. [X] has been previously submitted under 35 U.S.C. 154(d)(4).
7. [ ] Amendments to the claims of the International Aplication under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are attached hereto (required only if not communicated by the International Bureau).
   b. [ ] have been communicated by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.
8. [ ] An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. [X] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). **(unsigned -- 2 pgs.)**
10. [ ] An English lanugage translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 to 20 below concern document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [X] A FIRST preliminary amendment.
14. [ ] A SECOND or SUBSEQUENT preliminary amendment.
15. [ ] A substitute specification.
16. [ ] A change of power of attorney and/or address letter.
17. [ ] A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
18. [ ] A second copy of the published international application under 35 U.S.C. 154(d)(4).
19. [ ] A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. [X] Other items or information:
    1. Copy of International Preliminary Examination Report dated 29 May 2001

Express Mail Label No.: EM122093965US

531 Rec'd PCT/PTC 07 NOV 2001

U.S. APPLICATION NO. (If known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
10/030886	PCT/EP00/03513	PST6220P1US/2168

21. [X] The following fees are submitted:

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):

	CALCULATIONS PTO USE ONLY
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **$1040.00**	
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$890.00**	
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO **$740.00**	
International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$710.00**	
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) **$100.00**	
ENTER APPROPRIATE BASIC FEE AMOUNT =	$890.00
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
Total claims	12 - 20 =	---	x **$18.00**	$ ---
Independent claims	1 - 3 =	---	x **$84.00**	$ ---
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ **$280.00**	$ ---

TOTAL OF ABOVE CALCULATIONS =	$890.00
☐ Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2. +	$
SUBTOTAL =	$890.00
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f)).	$
TOTAL NATIONAL FEE =	$ 890.00
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +	$
TOTAL FEES ENCLOSED =	$ 890.00
Amount to be refunded:	$
charged:	$

a. ☐ A check in the amount of $ _____ to cover the above fees is enclosed.

b. [x] Please charge my Deposit Account No. 01-1350 in the amount of $ 890.00 to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [x] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 01-1350. A duplicate copy of this sheet is enclosed.

d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:
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34,054
REGISTRATION NUMBER

November 7, 2001

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:
LOSA, Riccardo

Docket No.: PST6220

Serial No.: Unassigned
Int'l Application No.: PCT/EP0003513
Int'l Filing Date: April 17, 2000
Priority Date: May 12, 1999

Group Art Unit:

Examiner:

Title: A COMPOSITION CONTAINING CARVACROL AND THYMOL FOR USE AS A BACTERICIDE

Assistant Commissioner of Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

In accordance with the provisions of 37 C.F.R. §1.111, applicants provide the following amendments and remarks for entry in the above-identified case.

IN THE SPECIFICATION

Please amend the specification as follows:

At page 1, after the Title, please insert the following:

--The present application was filed on April 17, 2000 as application serial number PCT/EP00/03513 and claims priority of Swedish patent application No. 9901733-7 filed on May 12, 1999.--

IN THE CLAIMS

Please cancel claims 2-10.

Please amend the claims as follows:

1. A composition which comprises the natural substances carvacrol in an amount of 5 ppm to 90% by dry weight, and thymol in an amount of 5 ppm to 80% by dry weight, the weight ratio between carvacrol and thymol being from 1:5 to 10:1.

Please add the following new claims:

--14. A medicament for the treatment of diseases caused by Treponema which comprises the composition of claim 1.

--15. The medicament of claim 14 wherein the weight ratio of carvacrol to thymol is from 2:3 to 4:1.--

--16. The medicament of claim 14, wherein said carvacrol and thymol are present in in amounts of 5-2000 ppm.--

--17. A method for treating swine dysentery which comprises administering an effective amount of the medicament of claim 14 to the affected swine.--

--18. The composition of claim 1 wherein the weight ratio between carvacrol and thymol being from 2:3 to 4:1.

--19. A diet composition which comprises the composition of claim 18, wherein said carvacrol and thymol are present in said diet composition in amounts of 5-2000 ppm calculated on dry weight of the diet composition.--

--20. The diet composition according to claim 19, which comprises 0.1-30 ppm calculated on the dry weight of natural substances, of at least one member selected from the group consisting of guaiacol, eugenol, capsascin and tannin, which enhance the health and increase the growth, and/or 0.2-50 ppm calculated on the dry weight of natural substances, of at least one member selected from the group consisting of creosol, anethole, deca-, undeca- and/or dodecalactones, quinoleine, ionones and/or irone, gingerol, piperine, propylidene and/or butylidene phtalides, amyl and/or benzyl salicylate.--

--21. A drinking water supplement which comprises the composition of claim 18 wherein said supplement comprises 2-90% by dry weight of carvacrol and thymol.--

--22. A drench bath supplement which comprises the composition of claim 18 wherein said supplement comprises 30-98% by dry weight of carvacrol and thymol.--

--23. A bactericide which comprises the composition of claim 1 in an amount to kill bacteria.--

--24 The diet composition of claim 19 wherein said carvacrol and thymol are present in said diet composition in amounts of 20-600 ppm calculated on dry weight of the diet composition.--

Remarks

This is an international application filed under the Patent Cooperation Treaty (PCT) on April 17, 2000. The examiner is respectfully requested to note that prior to the present amendment, claims 1-10 were pending in the present application as demonstrated by the International Preliminary Examination Report submitted herewith. In the present amendment, claims 2-10 are cancelled and new claims 14-24 are added to the application. New claims 14-24 correspond substantially with cancelled

claims 2-10. No new issues are raised by the amendments and it is believed that the claims are in ideal condition for U.S. prosecution.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Since the present amendment raises no new issues and presents no new matter, entry thereof in accordance with 37 C.F.R. §1.111 prior to the initial examination of the present case on the merits is respectfully requested.

Respectfully submitted,

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Version with markings to show changes made

The following sentence was added on page 1 of the specification after the title:

--The present application was filed on April 17, 2000 as application serial number PCT/EP00/03513 and claims priority of Swedish patent application No. 9901733-7 filed on May 12, 1999.--

Claim 1 was amended as follows:

1. A ~~Use of a~~ composition ~~containing~~ which comprises carvacrol in an amount of 5 ppm to 90% by dry weight, and thymol in an amount of 5 ppm to 80% by dry weight, the weight ratio between carvacrol and thymol being from 1:5 to 10:1~~, as an active agent for the manufacture of a medicament for treatment of diseases caused by Treponema~~.

The following new claims are added to the application:

--14. A medicament for the treatment of diseases caused by Treponema which comprises the composition of claim 1.

--15. The medicament of claim 14 wherein the weight ratio of carvacrol to thymol is from 2:3 to 4:1.--

--16. The medicament of claim 14, wherein said carvacrol and thymol are present in in amounts of 5-2000 ppm.--

--17. A method for treating swine dysentery which comprises administering an effective amount of the medicament of claim 14 to the affected swine.--

--18. The composition of claim 1 wherein the weight ratio between carvacrol and thymol being from 2:3 to 4:1.

--19. A diet composition which comprises the composition of claim 18, wherein said carvacrol and thymol are present in said diet composition in amounts of 5-2000 ppm calculated on dry weight of the diet composition.--

--20. The diet composition according to claim 19, which comprises 0.1-30 ppm calculated on the dry weight of natural substances, of at least one member selected from the group consisting of guaiacol, eugenol, capsascin and tannin, which enhance the health and increase the growth, and/or 0.2-50 ppm calculated on the dry weight of natural substances, of at least one member selected from the group consisting of creosol, anethole, deca-, undeca- and/or dodecalactones, quinoleine, ionones and/or irone, gingerol, piperine, propylidene and/or butylidene phtalides, amyl and/or benzyl salicylate.--

--21. A drinking water supplement which comprises the composition of claim 18 wherein said supplement comprises 2-90% by dry weight of carvacrol and thymol.--

--22. A drench bath supplement which comprises the composition of claim 18 wherein said supplement comprises 30-98% by dry weight of carvacrol and thymol.--

--23. A bactericide which comprises the composition of claim 1 in an amount to kill bacteria.--

--24 The diet composition of claim 19 wherein said carvacrol and thymol are present in said diet composition in amounts of 20-600 ppm calculated on dry weight of the diet composition.--

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A COMPOSITION CONTAINING CARVACROL AND THYMOL FOR USE AS A BACTERICIDE

The present invention relates to a composition containing the natural substances carvacrol and thymol. The composition exhibits a synergistic bactericidal effect against Treponema, which causes severe muco-hemorrhagic dieseases, such as swine dysentery and severe diseases affecting the hoofs of hoofed animals, particularly cloven-hoofed animals, such as ruminants. The composition is suitably administered to an animal via a diet composition, drinking water or a drench bath.

Diseases caused by Treponema are common in animal stocks. For example, an anaerobic spirochete, Treponema hyodysenteriae, is considered to be the primary etiologic agent of swine dysentery (SD). See for instance D.L. Harris and R.J. Lysons (1992), Swine dysentery, in: Diseases of swine, 7th edition, Iowa State University Press, Ames, Iowa, USA. SD is a severe muco-hemorrhagic diarrhoea. Pigs actually affected with SD usually consume very low amounts of feed causing an essential reduction in growth and a considerable economical loss. In Top Agrar (1998), Vol. 4, page 52 it is reported that in Germany one third of the piglets herds and as much as one half of the growing pig herds probably are Treponema-positive. Large efforts are therefore justified to prevent the diseases to be spread. It is also well known that Treponema causes severe diseases affecting the hoofs of hoofed animals, particularly cloven-hoofed animals, such as ruminants.

M. Tiziana Baratta et al.: "Chemical composition, antimicrobial and antioxidative activity of laurel, sage, rosemary, oregano and coriander essential oils" Journal of Essential Oil Research., vol. 10, no 6, 1998, pages 618-627, XP000929938 XX, XX ISSN: 1041-2905, disclose the chemical composition of five essential oils, derived from sage, rosemary, oregano, laurel and coriander, and also the anti-

bacterial activity of these essential oils against a number of microorganisms.

WO 96/37210 describes a pharmaceutical composition wherein the active agent is an extract from certain plants, especially Origanum vulgaris, Thymus vulgaris and Menta piprita. In general, the extracted oil contains 3% thymol and 60-70% carvacrol

Furthermore, in WO 97/01348 it is disclosed a pharmaceutical composition comprising a herbal essential oil containing thymol and carvacrol as its main ingredients and pharmaceutically acceptable carrier. The total amount of thymol and carvacrol in said essential oil is at least 55%, preferably 70% by weight of said essential oil, and the ratio of carvacrol to thymol is at least 10. This pharmaceutical composition can be used in the prevention and treatment of coccidiosis in poultry.

A wide spectrum of antibiotics, such as streptomycin, bacitracin, neomycin, tylosin, gentamycin, chlostetracycline, virginamycin and lincomycin, have been reported to be effective in the treatment of SD. Where the disease is endemic, preventive medication is often added to the animal feed. However, it seems that the antibiotics become less and less effective and Top Agrar (1998), Vol. 4, page 52, reports a resistance ratio of Treponema of 99% to tylosin, 92% to lyncomycin and 48% to tiamulin in 1997.

However, in recent years there has been an intense debate about the use of chemical and antibiotic growth promoters and in many countries a ban on this type of feed additives is being considered. Thus, there is an urgent need for agriculture to develop substances which are in line with reliable and generally accepted practice and not of a medicinal nature.

One objective of the present invention is to provide natural substances as active agents, which are suitable for the administration to the animal via a diet, drinking water or a drench bath for the cure, prevention or alleviation of the diseases caused by Treponema. Another objective is to reduce the negative effects on the growth.

According to the invention it has been found that a composition, containing the natural substances carvacrol in an amount of 5 ppm to 90% by dry weight and thymol in an amount of 5 ppm to 80% by dry weight, in a weight ratio between 1:5 and 10:1, preferably between 2:3 and 4:1, exhibits a synergistic effect against Treponema and thereby diminishing the negative effect these bacteriae have on the health and growth of animals. By the expression "a natural substance" is in this context understood a substance which consists of compounds occurring in nature and that is obtained from natural products or through synthesis. The composition is usually administered as a diet composition or as a drinking water containing carvacrol and thymol in amounts of 5-2000 ppm, preferably 20-600 ppm, calculated on the dry weight of the diet composition including nutritive

substances or on the weight of the drinking water. The composition may also be present in an amount of 0.2-30% by weight in a drench bath for the treatment of the hoofs of hoofed animals, particularly cloven-hoofed animals, such as ruminants. The invention also includes a premix and a diet additive that may be used in the preparation of the diet composition as well as a drinking water supplement and a drench bath supplement.

The composition and the diet composition may also contain other natural substances which enhance the health and improve the growth. In the diet composition these substances are normally present in an amount of 0.1 to 30 ppm, calculated on the dry weight. Examples of such substances and their amounts are 1-5 ppm guaiacol, 1-5 ppm eugenol, 0.1-2 ppm capsascin and 1-20 mg tannin. Other suitable ingredients in the diet composition are flavourings of natural substances. They are usually present in an amount of 0.2-50 ppm, calculated on the dry weight of the diet composition. Examples of suitable flavourings and their amounts are 0.05-0.5 ppm creosol, 0.1-5 mg anethole, 0.1-2 ppm of deca-, undeca- and/or dodecalactones, 0.1-2 quinoleine, 0.1-2 ppm ionones and/or irone, 0.05-1 ppm gingerol, 0.05-2 ppm piperine, 0.05-1 ppm propylidene and/or butylidene phtalides and 0.1-5 ppm amyl and/or benzyl salicylate.

The incorporation of active ingredients into the diet composition is usually carried out by preparing a premix of the active compounds carvacrol and thymol and other suitable additives. Such a premix may contain 1-10% by dry weight of carvacrol and thymol, 0-40% by dry weight of growth improving additives, flavourings and health enhancing additives, and 50-99% by weight of an absorbing support. The support may contain, for example, 40-50% by weight of wood fibres, 8-10% by weight of stearin, 4-5% by weight of curcuma powder, 4-5% by weight of rosemary powder, 22-28% by weight of limestone, 1-3% by weight of a gum, such as gum arabic, 5-50% by weight of sugar and/or starch and 5-15% by weight of water.

This premix can then be mixed with common feed components, such as vitamins, enzymes, mineral salts, ground cereals, protein-containing components, carbohydrate-containing components, wheat middlings and/or brans in the preparation of a diet composition additive which contains 0.2-5% by weight of the premix. The diet composition additive is then finally added to the diet composition in such quantities that the feed will contain 5-2000 ppm, preferably 20-600 ppm, of the active mixture. The diet composition additive normally constitutes 0.3-3.5% by weight of diet composition.

The diet composition according to the invention usually contains, calculated on the dry weight of the feed, the following ingredients:

a) 0-80%, preferably 10-70%, by weight of cereals,

b) 0-30%, preferably 1-12%, by weight of fat,

c) 0-85%, preferably 10-50%, by weight of protein containing nutritious substances of a type other than cereals, and

d) 1-500 ppm, preferably 10-100 ppm, of the mixture.

The total amounts of a)-d) are preferably at least 80% by weight.

When preparing the diet composition, the diet composition additive can be mixed with the dry ingredients consisting of cereals, such as ground or crushed wheat, oats, barley, maize and rice; vegetable protein feed based on e.g. rapeseed, soya bean and sunflower; animal protein feed, such as blood meal, meat and bone meal and fish meal; molasses; and milk products, such as various milk powders and whey powders. After mixing all the dry additives, the liquid ingredients and ingredients, which after heating become liquid, can be added. The liquid ingredients may consist of lipids, such as fat, for example slaughter fat and vegetable fat, optionally liquefied by heating, and/or of carboxylic acids, such as a fatty acid. After thorough mixing, a mealy or particulate consistency is obtained, depending on the degree of grinding of the ingredients. To prevent separation during storage, water should preferably

be added to the animal feed, which then is subjected to a conventional pelletising, expanding or extruding process. Any excess water can be removed by drying. If desired, the resulting granular animal feed can also be crushed to a smaller particle size.

The drinking water supplement may contain 2-90% by dry weight, preferably 10-50% by dry weight, of carvacrol and thymol. Beside carvacrol and thymol the supplement also contains 10-98% by dry weight of a large number of other ingredients. Common ingredients are mineral salts, vitamines, natural substances enhancing the health and growth, flavourings, water-soluble or water-dispersable carriers, such as sugars, powdered milk, milk-by-products and cellulose derivatives, dispersing agents and stabilisers, such as water-soluble or water-dispersable polymers. Suitable examples of natural substances enhancing the health and growth have earlier been described. When preparing the drinking water, the supplement is normally added to the water in such an amount that the concentration of the natural substance becomes 5-2000 ppm, preferably 20-600 ppm.

The drench bath supplement may contain 30-98% by dry weight of carvacrol and thymol and 2-70% by weight of mineral salts, water-soluble or water-dispersable carriers, dispersing agents and/or stabilisers, such as water-soluble or water-dispersable polymers.

Within the scope of the invention, it is also possible to produce a suspension of the diet composition. This is especially convenient if the feed is prepared for immediate consumption.

The present invention will now be further illustrated by the following Examples.

Example 1

The antimicrobial activity of the composition of the invention towards Treponema innocens and Triponema hyodysenteriae was determined in vitro. In the tests the following organisms, growth media, culture conditions and evaluation method were used.

Organisms: Treponema innocens, ATTC 29796
Treponema hyodysenteriae, ATCC 31212

Growth media: Caseine-peptone soymeal-peptone agar USP (Caso-Agar, Merch No. 5458) + 5% Sheep blood

Culture conditions: Anaerobic incubation at 37°C for 4-6 days

Evaluation method: Agar dilution test (according to DIN 58940, teil 6)

Agar plates were prepared by using the growth media, to which 10% by weight of a solution of carvacrol and/or thymol in polypropylene glycol had been added.

Cell suspensions with a concentration of 10.9 cfu/ml were prepared of each of the organisms. The single suspensions were then distributed on the agar surface using a Multipoint inoculator applying 1µl to a final surface of about 0.5 cm^2. For every concentration of carvacrol and/or thymol two parallel plates were inoculated and on each plate three inoculation points of each of the two organisms are applied. After the inoculation period the growth of the organisms were observed. If no growth was observed, the concentration of carvacrol and/or thymol was in the next test reduced to half. The minimum concentration of carvacrol and/or thymol leading to a total suppression of bacterial growth is noted as the MIC value (minimal inhibitory concentration) of the active components or compounds. The following results were obtained.

Table 1. Minimal inhibitory concentration

Test No.	Active compound	MIC value, ppm	
		Treponema innocens	Treponema hyodysenteriae
1	Thymol	625	625
2	Carvacrol	313	313
3	2/3 Thymol 1/3 Carvacrol	156	156
4	1/2 Thymol 1/2 Carvacrol	156	156
5	1/3 Thymol 2/3 Carvacrol	< 78	< 78

From the results it is evident that the composition of the invention exhibits a synergistic antimicrobial effect on the tested organisms.

Example 2

In order to determine the efficacy of the mixture of the invention to reduce the occurrence of Treponema some tests were performed with grower pigs (25 kg to 100 kg), which were put on commercial diets with the following composition.

Crude protein, %	24.0
Crude fat, %	6.0
Crude fiber, %	3.5
Crude ash, %	5.0
Lysine, %	1.35
MJDE, kg	14.3

This diet was formulated by mixing suitable amounts of wheat, lupin kernel, canola meal, rice pollard, meat meal, blood meal and tallow. To the diet administrated to the experimental group 100 ppm of a mixture containing 67 ppm carvacrol and 33 ppm thymol were added.

During the growing phase animal faeces were controlled for presence of Treponema and development of dysentery was recorded. The following results were obtained.

Table 2. Occurence of swine dysentery and Treponema in faeces

	No. of animals controlled	Presence of Treponema in faeces	Development of swine dysentery
Control	23	8	1
Experimental	10	0	0

These results clearly indicate that the occurrence of Treponema is much lower when the mixture of the invention is added to the feed in comparison to a negative control.

Example 3

The purpose of the following experiments were to investigate the effect of the mixture according to the present invention to increase animal growth and inhibition of the growth of Treponema. Forty male pigs in two pens were allocated to each treatment. The pigs were weighed individually at an age of 46 days, when the experimental diets were introduced. The experiment continued for 42 days. All the diets in the tests contained the following basic composition.

Crude protein, %	24.4
Crude fat, %	6.3
Crude fiber, %	3.5
Crude ash, %	5.3
Lysine, %	1.35
MJDE, kg	14.5

This composition was formulated by mixing suitable amounts of wheat, lupin kernel, canola meal, rice pollard, meat meal, blood meal and tallow.

In a control test A 100 ppm Olaquindox and 25 ppm Tiamulin had been added to the basic composition while in tests I and II according to the invention the diets contained 100 ppm and 200 ppm of the mixture of carvacrol and thymol disclosed in Example 2. In a control test B the diet consisted of the basic composition. The following results were obtained.

Table 3. Effect on the performance of pigs between 46 and 67 days of age.

Tests	A	B	I	II
Start weight (kg)	15.3	15.2	15.3	15.2
Final weight (kg)	28.6	27.0	26.9	27.2
Daily gain (g)	666	588	578	595
Feed intake (g/d)	1100	1000	933	971
Feed gain	1.65	1.70	1.61	1.63

Table 4. Effects on the performance of pigs during 67 to 88 days of age.

Tests	A	B	I	II
Final weight (kg)	42.8	41.9	40.8	41.2
Daily gain (g)	665	695	655	671
Feed intake (kg/d)	1.38	1.42	1.32	1.37
Feed gain	2.04	2.05	2.02	2.05

From these results one can clearly see that the addition of the mixture of the invention increases the growth especially in the period between 46 and 67 days of age.

The effect of diets containing the active mixture of the invention and the presence of Treponema in faeces was investigated by feeding four groups with five pigs in each group on the diets used in control test A and B and in tests I and II. The faeces of each pig was examined in regard to the presence of Treponema after the pigs have been fed on the diets 4, 8 and 16 days. The following results were obtained.

Table 5. Occurence of Treponema in faeces

	Samples with Treponema			
Time, days	**Control A**	**Control B**	**Test I**	**Test II**
4	1	3	4	4
8	3	3	0	0
16	0	0	0	0

From the results it is evident that the pigs fed on the diet according to the invention did not have Treponema in their faeces after 8 days while the pigs fed on the diets in Controls A and B needed treatment for 16 days.

CLAIMS

1. Use of a composition containing carvacrol in an amount of 5 ppm to 90% by dry weight, and thymol in an amount of 5 ppm to 80% by dry weight, the weight ratio between carvacrol and thymol being from 1:5 to 10:1, as an active agent for the manufacture of a medicament for treatment of diseases caused by Treponema.

2. Use according to claim 1, where the weight ratio is from 2:3 to 4:1.

3. Use according to claim 1 or 2, where the medicament is a diet composition containing carvacrol and thymol in amounts from 5 to 2000 ppm.

4. Use according to any one of claims 1-3 for the treatment of swine dysentery or for the treatment of the hoofs of hoofed animals.

5. A composition, **characterized in** that it contains carvacrol in an amount of 5 ppm to 90% by dry weight and thymol in an amount of 5 ppm to 80% by dry weight, the weight ratio between carvacrol and thymol being 2:3 to 4:1.

6. A diet composition according to claim 5, **characterized in** that it contains carvacrol and thymol in amounts of 5-2000 ppm calculated on dry weight of the diet composition.

7. A diet composition according to claim 6, **characterized in** that the diet composition contains 0.1-30 ppm calculated on the dry weight of natural substances, selected from the group consisting of guaiacol, eugenol, capsascin and tannin, which enhance the health and increase the growth, and/or 0.2-50 ppm calculated on the dry weight of natural substances, selected from the group consisting of creosol, anethole, deca-, undeca- and/or dodecalactones, quinoleine, ionones and/or irone, gingerol, piperine, propylidene and/or butylidene phtalides, amyl and/or benzyl salicylate.

8. A drinking water supplement according to claim 5, **characterized in** that it contains 2-90% by dry weight of carvacrol and thymol.

9. A drench bath supplement according to claim 5, **characterized in** that it contains 30-98% by dry weight of carvacrol and thymol.

10. Non-pharmaceutical use of a composition according to claim 5 as a bactericide against Treponema.

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(54) Title: A COMPOSITION CONTAINING CARVACROL AND THYMOL FOR USE AS A BACTERICIDE

(57) Abstract

The present invention relates to a composition containing the natural substances carvacrol and thymol. The amount of carvacrol is 5 ppm to 90% by dry weight, the amount of thymol is 5 ppm to 80% by dry weight, and the weight ratio between carvacrol and thymol is from 1:5 to 10:1. The composition exhibits a synergistic bactericidal effect against Treponema which causes severe muco–hemorrhagic diseases, such as swine dysentery and severe diseases affecting the hoofs of hoofed animals, particularly cloven–hoofed animals, such as ruminants. The composition is suitably administered to an animal via the diet or via the drinking water or via a drench bath.

Docket No.: **PST6220P1US/2168** PCT/US

DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: **A COMPOSITION CONTAINING CARVACROL AND THYMOL FOR USE AS A BACTERICIDE**

the specification of which:

☒ was filed on **17 APRIL 2000** as Appln Ser. No. **PCT/EP00/03513**

☒ and was amended on **05 MAY 2001** (if applicable)

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above. All factual statements made in the specification of my own knowledge are true and all factual statements made on information and belief are believed to be true.

I acknowledge to the duty to disclose information which is material to the patentability of this application in accordance with Title 37, Code of Federal Regulations, Sec. 1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, Sec. 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

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9901733-7	SWEDEN	12 MAY 1999	**X** Yes ____No
(Number)	(Country)	(Day/Month/Year)	

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I hereby claim the benefit under Title 35, United States Code, Sec. 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, Sec. 112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, Sec. 1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

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POWER OF ATTORNEY: As a named inventor, I hereby appoint the following as my attorneys of record, with full power of substitution and revocation, to prosecute this application and to transact all business in the Patent Office:

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